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### Polymerization of human prion peptide HuPrP 106-126 to amyloid in nucleic acid solution.

Nandi PK  
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#### Abstract

The human prion peptide PrP106-126 polymerizes in the presence of DNA both in its circular and linearized forms under solution conditions where the peptide alone does not polymerize. The polymerization process has been monitored by the increase in the fluorescence of anilino naphthalene sulfonic dye which detects the availability of the hydrophobic surface(s) in the aggregate as a consequence of polymerization. The polymerization is a nucleation dependent phenomenon as is evidenced from an existence of a lag period before the onset of the polymerization and a strong dependence of the polymerization on the prion peptide concentrations. The reaction is dependent on the pH as seen from rapid polymerization at pH 5 compared to the reaction at neutral pH where no polymerization is observed after a relatively long period of incubation. The polymer has been characterized as amyloid by using new absorbing and emitting species resulting from the interaction of the polymer with the amyloid specific fluorescent dye, Thioflavine S. This is probably the first demonstration that an endogenous macromolecule can influence the polymerization of a prion peptide. We have previously shown that there is a conformational change in the nucleic acid as a consequence of this interaction. This prion peptide is considered as a model to understand prion diseases as is evidenced from its toxicity towards primary brain cells in culture. The peptide encompasses one of the important amyloidogenic regions of the normal cellular prion protein. Demonstration of nucleic acid induced polymerization of the normal and scrapie prion isoforms accompanying a change in the nucleic acid conformation can establish a possible role of nucleic acid in prion disease.

#### MeSH

[Amino Acid Sequence](#); [Amyloid](#); [Anilino Naphthalenesulfonates](#); [Animal](#); [DNA](#); [Fluorescent Dyes](#); [Human](#); [Hydrogen-Ion Concentration](#); [In Vitro](#); [Macromolecular Systems](#); [Molecular Sequence Data](#); [Peptide Fragments](#); [Polymers](#); [Prion Diseases](#); [Prions](#); [Protein Binding](#); [Solutions](#); [Thiazoles](#)

are applied to an 5% polyacrylamide gel, electrophoresed for 3 hrs at 20V/cm in a 90mM Tris-borate buffer (pH 8.3), DNA fragments of a different mobility are clearly detectable for individuals without the 3 bp deletion, heterozygous or homozygous for the deletion.

As already explained with respect to Figure 20, the PCR amplified genomic DNA can be subjected to gel electrophoresis to identify the 3 bp deletion. As shown in Figure 20, in the four lanes the first lane is a control with a normal/ $\Delta$ F508 deletion. The next lane is the father with a normal/ $\Delta$ I507 deletion. The third lane is the mother with a normal/ $\Delta$ F508 deletion and the fourth lane is the child with a  $\Delta$ F508/ $\Delta$ I507 deletion. The homoduplexes show up as solid bands across the base of each lane. In lanes 1 and 3, the two heteroduplexes show up very clearly as two spaced apart bands. In lane 2, the father's  $\Delta$ I507 mutation shows up very clearly, whereas in the fourth lane, the child with the adjacent 507, 508 mutations, there is no distinguishable heteroduplexes. Hence the showing is at the homoduplex line. Since the father in lane 2 and the mother in lane 3 show heteroduplex banding and the child does not, indicates either the child is normal or is a patient. This can be further checked if needed, such as in embryoic analysis by mixing the 507 and 508 probes to determine the presence of the  $\Delta$ I507 and  $\Delta$ F508 mutations.

Similar alteration in gel mobility for heteroduplexes formed during PCR has also been reported for experimental systems where small deletions are involved (Nagamine et al supra). These mobility shifts may be used in general as the basis for the non-radioactive genetic screening tests.

### 5.3 CF SCREENING PROGRAMS

It is appreciated that approximately 1% of the carriers can be detected using the specific  $\Delta$ I507 probes of this particular embodiment of the invention. Thus, if an individual tested is not a carrier using the  $\Delta$ I507